the many helpful suggestions made at that time.

In view of the previous amendments to the claims it was believed that the claims in their present form meet all the requirements of 35 U.S.C. 112 and further comment in connection therewith should not be necessary. Reconsideration of all the claims in the application is respectfully requested for the reasons set forth below.

Claim 1 and 8 to 10 have been rejected under 35 U.S.C. 103 as being unpatentable over Lafon I or II. This rejection is respectfully traversed.

The Examiner again maintains that:

> "the references disclose the racemate of the claimed levorotatory compound, therapeutic compositions thereof and useful in treatment of awakening disorders and of confusion especially in the elderly. The claimed optical isomer would be obvious from the racemate containing it in the absence of any unobvious properties. It would be quite obvious to use the particular optical isomer which had the greater activity".

In response to Applicant's arguments presented in the paper filed December 14, 1988, the Examiner contends:

> "The mere fact that the levorotatory compound has a better bioavailability which is not predictable is not unexpected.

Since the levorotatory and racemic mixture thereof have the same utility - it is not surprising that one of the numbers of the racemic mixture alone has a far greater activity than the racemic mixture itself since usually the racemic mixture owes its activity to the member which exhibits the activity in question".

Lafon I, U.S. Patent 4,177,290, discloses as noted by the Examiner, the racemate compound (|)-benzhydryl-sulfinylacetamide which is coded as CRL 40 476. The reference (see column 7, lines 18-19) shows that "CRL 40 476 did not alter the length", that is, duration "of the barbituate induced sleep".

Lafon II, EPA 0 097 071, is concerned with derivatives of the racemate which comprises at least one substitutent either on one of the two phenyl rings or on the nitrogen atom. Said substituted compounds provoke a significant decrease in the sleep duration induced by pentobarbital, as explained on page 4, lines 1-10 and table IV of the publication. It should be noted that the translated abstract of EP-A - 0 097 071 is incorrect when it indicates that the comparison product (i.e. CRL 40 476) increases the duration of sleep since such an increase is not supported by the comments of the above noted page 4.

The levorotatory isomer which is coded as CRL 40 492, differs form the racemate, CRL 40 476, and from the dextrorotatory isomer, CRL 40 493 in a number of

surprising and unexpected ways, as discussed in detail in the specification. Its metabolism is different, as shown by the comparative assay given in the disclosure, (see section "PHARMACOKINETIC STUDY" appearing at page 8 line 26 to page 10, line 33 and table II of page 12). Such comparative assays surprisingly show that isomer CRL 40 982 of the invention exhibits an unobvious bioavailability when administering in vivo, in comparison to the racemate CRL 40 476 and dextro isomer CRL 40 983. In view of these results, it would not be necessary to determine whether or not CRL 40 982 provokes an increase or a decrease in the duration of the pentobarbitol induced sleep.

Moreover, as discussed in the present specification at page 7 to page 8 and during the aforementioned interview, in connection with toxicity, behavior in rats and effect on motor activity in mice, the experimental results show that the levo isomer is clearly unexpectedly different than either the racemic compound or the detro isomer.

The levo isomer is significantly more toxic as discussed at page 7, although the significantly greater toxicity of the levo isomer does not present a problem within the useful range of non-lethal concentrations.

The differences in stimulant effects of different doses of the levo isomer compared to those for the detro isomer and racemic compounds on rats as discussed at pages 7-8 were certainly unexpected as are the effects found under experimental conditions in the comparative tests reported with regard to various doses on mice as discussed at page 8. It is believed to be clear from the results of the experimental conditions reported, that the effectiveness achieved specifically with the levo isomer in comparison with those determined for the detro isomer and racemic compound are surprising and unexpected.

Moreover, as pointed out previously as well as during the aforementioned interview, the use of the isomer of the invention, CRL 40 982, in the treatment of Alzheimer's disease as defined in claims 4 hereof is neither desclosed nor even remotely suggested by Lafon I or Lafon II. "Memory disorders" and "confusion" are generally similar effects but are not the only characteristics of, for example, Alzheimer's disease, and transient effects are not indicative of the permanent memory disorders and confusion that are experienced by one afflicted by such a disease.

It is respectfully submitted that applicant has made a significant invention of which there is no counterpart or even the suggestion in any of the references of record. The claims as presented herein carefully define the present invention, are proper in

form and are fully supported by the application as filed. Reconsideration of the specification and claims in their present form, and early and favorable action is, accordingly courteously solicited.

Respectfully submitted,

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